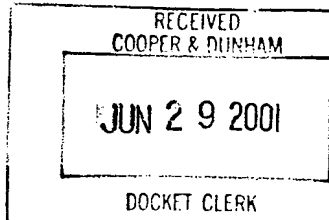


PATENT COOPERATION TREATY

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From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: JOHN P. WHITE
COOPER & DUNHAM LLP
1185 AVENUE OF THE AMERICAS
NEW YORK, NY 10036



PCT

WRITTEN OPINION

(PCT Rule 66)

Reply to Written Opinion: 7/26/2001 ^{SME}

Date of Mailing (day/month/year) **26 JUN 2001**

Applicant's or agent's file reference

58040-A-PCT

REPLY DUE

within ONE months
from the above date of mailing

International application No.

PCT/US00/12536

International filing date (day/month/year)

04 MAY 2000

Priority date (day/month/year)

04 MAY 1999

International Patent Classification (IPC) or both national classification and IPC
IPC(7): A61K 38/16 and US Cl.: 514/2, 21

Applicant

THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK

1. This written opinion is the first (first, etc.) drawn by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

3. The applicant is hereby invited to reply to this opinion.

When? See the time limit indicated above. ~~The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).~~

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 *bis*.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 04 SEPTEMBER 2001

Name and mailing address of the IPEA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

Christina Lawrence Fox
JEAN C. WITZ

Telephone No. (703) 308-0196

WRITTEN OPINION

International application No.

PCT/US00/12536

I. Basis of the opinion

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed

☒ the description:

pages 1-34 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

☒ the claims:

pages 35-37 , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

☒ the drawings:

pages 1-9 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

☒ the sequence listing part of the description:

pages NONE , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

☒ the description, pages NONE

☒ the claims, Nos. NONE

☒ the drawings, sheets/fig NONE

5. ☐ This opinion has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed".

WRITTEN OPINION

International application No.

PCT/US00/12536

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. statement**

Novelty (N)	Claims <u>1-21</u>	YES
	Claims <u>NONE</u>	NO
Inventive Step (IS)	Claims <u>1-21</u>	YES
	Claims <u>NONE</u>	NO
Industrial Applicability (IA)	Claims <u>1-21</u>	YES
	Claims <u>NONE</u>	NO

2. citations and explanations

Claims 1-21 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the use of a gp130 receptor ligand and a growth factor to induce mesenchymal precursor cells to differentiate into kidney epithelia.

----- NEW CITATIONS -----
NONE

WRITTEN OPINION

International application No.

PCT/US00/12536

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

<u>Application No. Patent No.</u>	<u>Publication Date (day/month/year)</u>	<u>Filing Date (day/month/year)</u>	<u>Priority date (valid claim) (day/month/year)</u>
WO, A, 0041713	20 JULY 2000	28 DECEMBER 1999	29 DECEMBER 1998

2. Non-written disclosures (Rule 70.9)

<u>Kind of non-written disclosure</u>	<u>Date of non-written disclosure (day/month/year)</u>	<u>Date of written disclosure referring to non-written disclosure (day/month/year)</u>

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1-21 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because practice of the claimed invention is not enabled as required under PCT Rule 5.1(a) for the reasons set forth in the immediately preceding paragraph.

The specification indicates that a combination of a gp130 receptor ligand, specifically LIF, in combination with a growth factor, most specifically TIMP, resulted in epithelialization of metanephric mesenchyme and formation of tubules and nephrogenesis in vitro. This has confirmed the state of the art that LIF alone has little effect in vitro on growth or on ureteric-bud morphogenesis other than to stimulate the bifurcation process. The state of the art also acknowledges that renal mesangial cells both synthesize and react to LIF. LIF is not mitogenic for the mesangial cells. LIF is excreted in the urine of kidney transplant patients undergoing acute rejection but is not found in stable graft recipients. Transgenic mice that overexpress LIF develop mesangial proliferative glomerulonephritis. While numerous growth factors have some influence on kidney development, the state of the art indicates that the specification has shown a developmental effect on kidney mesangial cells of LIF combined with TIMP, such showing is insufficient to enable claims to in vivo treatments of kidney disease and failure. It remains unpredictable as to the interactions of the growth factors with the extant kidney tissue as well as the response of the transplanted primordial kidney tissue when exposed to the in vivo biochemistry and physiology. This is particularly true of claim 4 and those claim that depend from same as there is no showing or suggestion of is supposed to occur when the LIF and the TIMP are administered. It would appear that the etiologies of the different types and causes of the kidney failure would be expected to have an effect upon how that kidney failure is treated. Therefore the cited claims are not enabled by the specification.

WRITTEN OPINION

International application No.

PCT/US00/12536

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

TIME LIMIT:

The time limit set for response to a Written Opinion may not be extended. 37 CFR 1.484(d). Any response received after the expiration of the time limit set in the Written Opinion will not be considered in preparing the International Preliminary Examination Report.

JPW

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: JOHN P. WHITE
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NEW YORK, NY 10036

RECEIVED
COOPER & DUNHAM

JUN 29 2001

DOCKET CLERK

PCT

WRITTEN OPINION

(PCT Rule 66)

Applicant's or agent's file reference 58040-A-PCT		Date of Mailing (day/month/year)
REPLY DUE within ONE months from the above date of mailing		
International application No. PCT/US00/12536	International filing date (day/month/year) 04 MAY 2000	Priority date (day/month/year) 04 MAY 1999
International Patent Classification (IPC) or both national classification and IPC IPC(7): A61K 38/16 and US Cl.: 514/2, 21		
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Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer <i>Christina Lawrence Fox</i> JEAN C. WITZ
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196